ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

Location of Meeting
Frontier Building, 3601 C Street, Room 880-890

MINUTES OF
September 17, 2004
8:00 a.m.
as approved on 10-29-04

Committee Members Present:
Marvin Bergeson
Michale Boothe
Heidi Brainerd
Richard E. Brodsky (Chairman)
Robert H. Carlson
Kelly C. Conright
Charlene M. Hampton
Arthur S. Hansen
R. Duane Hopson
Thomas K. Hunt
Diane Liljegren (telephonic)
Ronald J. Miller
Gregory P. Polston
Sherrie D. Richey
George Stransky
Alexander H. vonHafften
Trish D. White

Committee Members Absent:
Jeffrey G. Demain
Traci Gale
Nathaniel Haddock
Ronald Keller
Janice L. Stables

Others Present
Dave Campana
Terry Babb
Verner Stillner
David Samson

I. CALL TO ORDER:

Chairman Brodsky called the meeting to order at 8:05 a.m.

II. ROLL CALL:

The roll call was taken and a quorum was present.

III. INTRODUCTION OF NEW MEMBERS:

Chairman Brodsky noted that there were two new members: Dr. Ron Keller, who was absent, and Dr. Marvin Bergeson.

Chairman Brodsky said a Mental Health Committee had been formed to review drugs that dealt with mental health issues. Dr. Stillner and Dr. Samson were present at the meeting.

Chairman Brodsky reviewed the process. The committee was charged with reviewing various drug classifications in an attempt to develop a Medicaid preferred drug list. This is not a formulary, but a preferred drug list. If a provider felt their patient needed a drug that was not on the preferred drug list, they could prescribe the drug by writing "medically necessary" on the prescription. No one is denied access to any prescribed medication. The preferred drug list is a way to encourage people to use drugs that are available to the State at a lower cost. The committee reviews the various classes to determine which drugs should be on the preferred drug list. First Health bids with the manufacturers for the best price, including available rebates. The committee hears presentations from various drug manufacturers to help them decide which drugs should be on the preferred drug list. After the preferred drug list is published, no patient will be denied the option to receive a non-preferred medication if their physician feels it is medically necessary. First Health is the fiscal intermediary and runs the program for the State. Some people felt First Health was not objective, so this year we contracted with the Oregon Center for Health Based Policy, which is an independent group that does similar reviews. We will utilize their information on drug classes when available. There is a public comment session at the beginning of the meeting. Each speaker receives five minutes to speak regardless of how many drugs they are discussing. The public comment session is scheduled for 45 minutes, but may need to be extended due to the number of speakers signed up today. Public comments are taken at the beginning of the meeting rather just before reviewing the drug classification, which the committee might want to review for future meetings.

The board discussed the public comment portion of the meeting. Thomas Hunt supported having the public comments prior to reviewing the drug classifications. Gregory Polston felt extra time should be given to representatives reviewing multiple drugs. Alexander vonHafften felt it would be more useful to have public comments prior to the discussion of the classification. Diane Liljegren said the committee did not always have time to review all the classifications on the agenda, so it would be more time efficient to hear the public comments before reviewing a specific classification.

THOMAS HUNT MOVED TO SEPARATE PUBLIC COMMENTS BY CLASSIFICATION FOR FUTURE MEETINGS. SECONDED BY MARVIN BERGESON. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

Chairman Brodsky asked for discussion on the time allotted to each speaker during the public comment period. Thomas Hunt felt more time should be given to those reviewing multiple drugs. Dave Campana pointed out the possibility of hearing from one speaker six different times if they reviewed drugs in six different classifications at a meeting.

THOMAS HUNT MOVED TO ALLOW INTERESTED PUBLIC PARTIES TO COMMENT MULTIPLE TIMES, ONE CLASSIFICATION AT A TIME. SECONDED BY ALEXANDER vonHAFFTEN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION.

The board discussed the motion. Robert Carlson said the committee could potentially spend the whole day listening to testimony, so they should establish a time limitation. Chairman Brodsky said they currently allowed 45 minutes for public comments and suggested setting a lower time limit for public

comments before each classification. Alexander vonHafften said the committee could review fewer classifications per meeting. Gregory Polston felt they should keep it as open as possible so each person had an opportunity to comment. Chairman Brodsky suggested setting a 30-minute period before each classification for public comments with a five-minute limit per person.

THOMAS HUNT MOVED TO LIMIT PUBLIC DISCUSSION FOR EACH CLASSIFICATION TO 30 MINUTES, FIVE MINUTES PER SPEAKER, WITH CHAIR DISCRETION TO EXTEND THE PUBLIC COMMENT PERIOD AS NECESSARY. SECONDED BY GEORGE STRANSKY. CHAIRMAN BRODSKY CALLED FOR DISCUSSION OF THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

Chairman Brodsky reviewed what the committee had achieved to date. The program has been very successful. We have spoken with the community, interest groups and physicians, including the State Medical Association, the Anchorage Medical Society and the Alaska Psychiatric Association, to educate people on the program. The rate of compliance with the preferred drug list is over 80 percent and there have been very few negative comments. The State is saving money and things are moving fairly smoothly. We are interested in listening and responding to the public's issues. The program has been modified to make it user-friendly and meet people's needs.

Terry Babb discussed what would be reviewed at future meetings. On October 22, 2004, they would review CoxII Inhibitors, Serotonin Receptor Agonists, Topical Immuno Modulators, Cholinesterase Inhibitors, Urinary Tract Anti-spasmodic and COPD Anti-cholinergic. On November 19, 2004, they would review the Anti-emetics, Leukotriene Modifiers, a Miscellaneous or Combination Anti-cholesterol Anti-hyperlipidemic class, and a re-review of the Proton Pump Inhibitors and the Angiotensin Receptor Blockers.

Chairman Brodsky said the committee would begin re-reviewing classes in November, which would be discussed later in the meeting.

IV. PUBLIC COMMENTS:

Representative Lesil McGuire said she appreciated the committee's work. It is important for everyone to receive appropriate health care and for physicians to have the ability to prescribe the drugs that they feel will benefit their patients. The life of the P&T Committee is short when compared to that of the regulators and the lawmakers. She had to fight hard in the senior care legislation to add a statute to allow for medically necessity. She was concerned with mental health patients. It is often difficult to identify which particular drug will have an overall health impact on one mental health patient versus another. Forcing a mental health patient into a particular preferred drug list may have no detrimental effect on that particular patient. As a whole, these are some of the most sensitive cases in our community. When you look at the statistics on crimes and criminals, a very high percentage of those people come from the mental health community. The committee should consider the fact that mental health patients are a special class of people. We do have the provision for medically necessary overrides, but it is not that simple when it plays out in the Legislature. She was concerned that regulators might come back behind the P&T Committee and limit doctors' abilities to have that very private and important relationship with their patients to make the kinds of decisions that they need to prescribe the appropriate drugs.

Amir Karimzadeh, Forest Research Institute, discussed Lexapro. They were looking for increasing compliance for mental health patients. To achieve that, you need better or equal efficacy, better side effect profiles and better dosing so patients will comply better. The data indicates we have at least as good, or better, efficacy as other SSRIs or SNRIs. Lexapro has a better side effect profile than other SSRIs. According to clinicians, compliance with Lexapro has significantly increased due to ease of dosing, which has a dose range. Lexapro has a 10 to 20 milligram dosing and increasing it to 20 milligrams is a one-step process. Therefore, you are increasing compliance by lowering the number of office visits and health care dollars. The safety profile and the drug-drug interaction speak very highly of Lexapro. There has been some significant advances made from its parent product. Lexapro has multiple indications. Lexapro has indications for MDD and GAD. It will soon have indications for SAD, as well as other indications we are pursing. Lexapro will be one of the few SSRIs that has multiple indications, favorable safety data and easy dosages for patients.

Beth LaCrosse said she was representing the Alaska Recovery and Choice Coalition, which consisted of a variety of female health providers, consumers and advocates. She did not want to speak about any specific drug classification, but the right physicians and consumers to have choices. She was currently a mental health consumer who had been on various medications and it took quite a few before she started to respond. The Coalition felt it was critical to allow choices in the preferred drug list to allow a patient to find the medication that works for them. It is important for the state to realize that we cannot balance the budget on the backs of the elderly, children and disabled persons of Alaska. The Coalition is advocating that psychotropic drugs not be held to a specific preferred drug list. As co-chair of the Coalition, as well as a mental health consumer, she felt allowing choice for both physicians and patients was very important.

Chairman Brodsky noted that this was a preferred drug list and not a formulary. They were listening to the consumers and no drugs were banned from use. They wanted to utilize the evidence to reduce variations and lower costs where possible. No citizen will be denied the use of a drug that their physician feels is medically necessary.

Roy Palmer, Pfizer, discussed Lipitor in the Statins class. Lipitor has a large body of clinical trial data for safety and efficacy in a broad range of patients, across the whole dose range. We have a great deal of safety and efficacy data at 80 milligrams, which is the highest approved dosage. In primary prevention, the Ascot Trial was stopped nearly two years early because of a significant benefit. The reversal study, which showed intra-vascular ultrasound, showed Lipitor could actually stop the progression of atherosclerosis. The Prove-It Trial for acute coronary patients is the only head-to-head trial in the class of Statins with mortality as an outcome. An aggressive treatment with Lipitor showed superiority over a less aggressive treatment protocol with Pravachol. This landmark trial led to the suggestion that we should be looking lower goals, as low as 70, for these high-risk patients. The Cards Trial showed a 36% reduction in vascular disease and a 48% reduction of stroke for diabetic patients. A large clinical study done by Eugene Brownwald is similar to the Prove-It Trial, but with Zocor. We saw there a neutral result that was in direct contrast to the Prove-It results. Not only was it a neutral result overall, but in the first four months there was actually a larger difference in the LDL levels achieved than in the Prove-It trial. We saw no benefit of aggressive treatment with Zocor and some doubt was cast on the safety of high doses of Zocor. He asked the committee to recommend Lipitor as the preferred drug in the Statin class while considering Lipitor's powerful LDL reductions and the large body of data on both efficacy and safety.

Booker Evans, a staff psychiatrist at the Good Samaritan Mental Health Center, discussed serotonin reuptake inhibitors, which he used daily. His drug choices were made based on patient presentation by matching the drug to the diagnosis. He felt there should be an unlimited formulary for these drugs. He used Zoloft about 50% of the time, Paxil and Lexapro about 25% of the time and the remaining drugs about 25% of the time. Patient population drives your choice of drugs. He works with abused women and sees a lot of post traumatic stress disorder and major depression, which requires a serotonin blocker to relieve depression and anxiety. Zoloft is a very effective drug, as is the other drugs. In terms of remission and relapse, Zoloft is a good drug, because you have fewer costs associated with hospitalization and suicide attempts. He felt the preferred drug list should remain an unlimited formulary.

Randy Howard, Glaxo Smith Kline, said he had been working with Wellbutrin and the psychiatry community in Alaska for the last 14 years. Major depression is second only to ischemic heart disease in the amount of disability experienced by suffers. In the year 2000, the total cost associated with major depression was estimated at $83.1 billion dollars. Lost productivity and absenteeism accounted for 62% of the total while mortality and direct treatment costs accounted for 7% and 13% respectively. Acute phased depression should be treated for 90 days with effective continuation treatment being 180 days per the National Committee for Quality Assurance based on the American Psychiatric Association and the Agency for Health Care Policy and Research Guidelines. Medication adherence is paramount to the successful treatment and overall improvement of patients. Dosing schedules and adverse events dramatically impact medication adherence for long-term treatment. Wellbutrin XL offers patients and doctors very distinctive benefits over any other bupropron formulations. The morning dose of Wellbutrin XL provides 24 hours of bupropion plasma concentrations while eliminating evening spikes in blood levels. Wellbutrin XL is the only once daily norepinephrine dopamine reuptake inhibitor indicated for the treatment of depressions and is a pregnancy category B. This means better patient compliance with once daily dosing that gives therapeutic blood levels of medication for 24 hours. Studies have shown that 37% of patients taking Wellbutrin SR fail to take their second dose and many try to take both doses at the same time. In either case, this leaves the patient trying to get by on half the effective therapeutic dose, not to mention the added potential for adverse advents. By eliminating the second dose, sleeping disturbances have been minimized. There are many strong supporters of Wellbutrin XL who can speak to the fact that Wellbutrin XL once daily, versus twice daily, has made significant improvements in patient compliance, efficacy, and decreased side effect complaints. It also cuts nursing and staff time in half for dispensing medications. The APA has stated that all of the new generation antidepressants have similar efficacy in the treatment of depression and the key to success is minimizing side effects and getting patients to comply with the treatment regimens. Not all products work the same on all patients, so it is important to have all these products available to doctors and practitioners to help their patients lead productive and mentally healthy lives. The difference between Paxil IR and Paxil CR is the way the product is absorbed by the body. The CR formulation is absorbed in the intestine, bypassing the stomach. Since reuptake inhibitors line the stomach, patients often experience nausea as a side effect of their medication. In the process of bypassing the stomach, the CR formulation is often better tolerated and therefore adhered to on a much more successful basis. Studies have shown that Paxil CR is associated with 25% lower risk of discontinuation versus the IR formulation. When comparing the two formulations, CR reduces the risk of switching medications or augmenting with other medications by 16% as compared to Paxil IR. Please consider including Wellbutrin XL and Paxil CR on the preferred drug list so our doctors have the most effective tools available to help their patients lead full and productive lives.

Dale Groth, Wyeth Pharmaceuticals, discussed Venlafaxine (Effexor). Venlafaxine is the first marketed serotonin norepinephrine reuptake inhibitor (SNRI) antidepressant in the U.S. It has been on the market for over ten years and has been prescribed for over 10,000,000 patients around the world. We have a wealth of evidence based scientific evidence behind its safety and efficacy in a wide range of patients and ages. Venlafaxine is approved for the short-term treatment of both major depressive disorder as well as two of the most common anxiety disorders, GAD and SAD. It is also approved for the long-term relapse prevention in patients diagnosed with major depressive disorder as well as recurrent major depressive disorders. Historically, all antidepressants have been deemed equal in efficacy for the treatment of major depressive disorders. Beginning in the late 1980s, some clinical trial data from the Netherlands indicated there may be efficacy differences between antidepressants that had a dual mechanism of action that has increased both serotonin and norepinephrine as compared to antidepressants that only increase serotonin or single action. More recently, there have been systematic reviews that compare the efficacy of Venlafaxine to certain studied selective serotonin reuptake inhibitors. These studies continue to show a signal that there may be a slight efficacy advantage in some patients in terms of the treatment of major depression. More studies need to be done to confirm the meta-analysis' initial signal findings. In terms of metabolism and drug interaction potential, Venlafaxine metabolites to an active compound called ODV and has an equal potency and efficacy to the parent compound. We have done extensive studies in patients, as well as laboratory based studies, and found that Venlafaxine is neither an inducer or inhibitor of the key enzymes. Therefore, the potential for drug-drug interactions tends to be low. It also has very low protein binding at about 30% as compared to 95% for most antidepressants. Venlafaxine should not be used concurrently with MAO inhibitors due to the potential for serotonin syndrome, which is true for all the SSRIs. Venlafaxine is associated with a sustained increase in blood pressure in some patients. Pre-marketing clinical trials have found that in .5% of GAD studies and 1.4% of SAD patients and 3% of patients with major depressive disorders. It is recommended that blood pressure monitoring be done while using Venlafaxine.

Dr. Miles Hassell, Bristol Myers Squibb, discussed Pravachol. He treated people with cardiovascular disease everyday and when they had a bad outcome, it made him look bad. A preferred medication for cardiovascular disease needs to satisfy fairly rigorous requirements and it should be safe and well studied. Pravachol has evidence for mortality reduction in both primary and secondary prevention rolls. There are only two Statins that qualify in that way. There is no more rigorous requirement than you can make for a cardiovascular drug than total mortality reduction. Pravachol has the largest body of evidence, including studies of 9,000 people for nine years. In terms of long-term safety, we have good evidence that Pravachol is an excellent drug. Special groups are also important. Part of the safety issue is that Pravachol is metabolized uniquely. This is critical for important subgroups of patients, because there are many drugs that are not used in Statin trials. For safety issues, the absence of metabolism through the cytochrome P-450 system is an important reason to include Pravachol on the preferred drug list. We have reason to suspect that there might be a safety advantage to Pravachol for people with HIV and the transplant population. He urged the committee to include Pravachol on the preferred drug list for the following three reasons: its mortality reduction, large numbers of people studied for long periods of time and the application of Pravastatin to specific groups.

Anne Morris, Cephalon Pharmaceuticals, said as a practicing sleep disorders physician for over 20 years, she wanted to address sedative/hypnotics and stimulants. She asked the committee to consider the non-benzodiazepine sedative/hypnotics, particularly in the practice in insomnia. Their main advantage is their shorter onset and offset of action, which allows us to encourage the patients to try non-pharmacological techniques first to try to fall asleep. If those were unsuccessful, there would still be

time to take a sedative if needed, because the newer agents have a more rapid offset action and the patient will not be sedated in the morning. That is not true with most of the benzodiazepines hypnotics. Therefore your patients tend to use less medication and not look at this as the only solution to their insomnia. Provigil (Modafinil) is not literally a stimulant and does not belong in this classification, but we do not know where else to put it. The exact mechanism by which Modafinil produces wakefulness is unknown. It appears to involve the hypothalamus and not the dopamine systems, so the addiction potential with most of the stimulants is not present. The drug is not a direct or indirect-acting dopamine receptor agonist. Modafinil has been successfully used in Europe since 1988 and was approved for use in the U.S. by the FDA in 1989. Its main indication is narcolepsy. The American Academy of Sleep Disorders Medicine says it is the drug of choice for the initial treatment of narcolepsy patients. Narcolepsy is a small percentage of the population, but Provigil is also useful in the treatment of other causes of EDS. It is now also approved by the FDA, because of its very low side effect profile and excellent effectiveness, for the treatment of residual sleepiness, EDS in patients with obstructive sleep apnea and alertness for shift workers. There are 70 million Americans that work non-traditional shift hours. Sleepiness is the leading cause of many car and other accidents. It has been increasingly used for the additional residual fatigue and sleepiness in depression. Neurologists are finding it extremely helpful in the debilitating fatigue and sleepiness of many of their patients with Multiple Sclerosis and Parkinson's Disease. It is now being investigated for use in ADHD. It has a weight neutral profile. The side effect profile is minimal, even in cardiac patients.

Tracy Durgin, Novartis Pharmaceuticals, discussed Ritalin LA, a stimulant to treat ADHD. ADHD is one of the most common neuro developmental disorders, which places substantial duress on patients, their families, employees, societies and health care systems. Untreated and under treated, ADHD exacts a tremendous toll on the patient's academic function, interpersonal relationships, professional successes and emotion wellbeing. Stimulants are the standard therapy for treating ADHD. Ritalin LA is the most widely prescribed stimulant in this class. Stimulant therapy is effective in reducing the core ADHD symptoms of inattention and hyperactivity. It reduces some of the negative impairments associated with ADHD as development progresses. Currently there are three products on the market: Ritalin LA, Concerta and Menadate CD. Each of these products utilizes a different drug delivery technology and has a unique profile. Ritalin LA delivers methylphenidate via a virodal drug absorption system. This system delivers 50% of the medication immediately upon administration, while 50% of the total daily dose delays. Concerta delivers 28% of the medication immediately while 72% is delayed. Menadate CD delivers 30% of the medication immediately while 70% is delayed. Since each of these products have such a unique profile and clinical profile, it would be in the best interest of the Alaska community to have more than one of these medications available on the preferred drug list. There are three distinct advantages to Ritalin LA that should be considered. Ritalin LA utilizes the unique drug delivery mechanism that mimics twice daily administration resulting in a rapid onset, providing coverage throughout the day while offering the convenience of a once daily dosing. Ritalin LA comes in four dosing strengths. Ritalin LA offers the advantage of (indiscernible) option for children who are not able to swallow pills.

Aleen Smith, Southcentral Counseling Center, said she has suffered from major depression for many years. Earlier someone testified that 81.2 billion dollars was lost to major depression. $500,000 of that is lost to loss of productivity. She was licensed to practice law in the State of Alaska, but has not been able to do so for a number of years. She was first hospitalized long-term with major depression in 1988 and have been going down hill ever since. During the 12 years between 1988 and 2000, none of the medications worked. In 2000, she was put on Wellbutrin. Despite the describing protocols for these drugs, doctors do not know what is going to work on an individual patient and they have to keep trying

different drugs. Several speakers describe prescribing drugs as either an artist's pallet or playing a chord on a piano. I feel it is more like a crap-shoot. We just don't know what is going to work. None of the drugs should be eliminated from the preferred drug list. The Common Wealth of Massachusetts decided that psych meds could not be messed with and they convinced the Legislature of that. As a result, the consumers have no concerns about whether or not their doctor is going to be able to experiment long enough to get them the right drug. Dr. Hanson assured us that by writing "medically necessary" on the prescription, doctors could use any drugs they wanted to. Lesil McGuire warned us earlier today that is not as simple as it sounds, because of potential Legislative problems. There is a clerk sitting down there in North Carolina who reviews Medicaid billings. Writing "medically necessary" on a prescription is not going to have a magic effect on the clerk that works for First Health in North Carolina. These prescriptions are going to be questioned over and over again. We do not want any psych meds left off the preferred drug list, because the doctors have to have the tremendous variety of medications available to find the correct medication for their patients.

Sharon Lubaugh, NAMI Juneau, discussed antidepressants. She felt allowing physicians to write "medically necessary" on prescriptions to use drugs not on the preferred drug list was the key to a successful plan. At a conference, a doctor explained to us that one of the biggest problems in prescribing drugs for the mentally ill was the fact that the brain is the organ in which everything has to happen. We do not have many brains in the animal work that are similar to humans that we can experiment on. So prescribing drugs for the mentally ill takes more experimentation by the physician to find the correct medication or combination of medications for their patients.

Karen Bryan, program manager at Polaris House, said she was a recovering drug addict who had used illegal drugs for 15 years. (Indiscernible -- telephonic.) Once a mentally ill patient finds the right mediation, they can be a responsible member of society.

Stephen Luber, a private practitioner in Spokane, Washington, said he spent much of his time working with behavior pediatrics and has done trials with many of the medications used for ADHD. Straterra should be placed on the preferred drug list. Straterra is an alternative to a class of medication that we know work well, have a long history of safety and have significant side effects that prevent their effective use in many situations. We can effectively treat the symptoms of ADHD, but we are often spending most of our time combating the problems of weight loss and sleeping difficulties that is associated with the use of stimulants. We are also finding increasing levels of problems with diversion of stimulants for recreational uses. We recognize that the use of stimulants dramatically reduces the incidences of substance abuse in the person with ADHD, if treated effectively, but diversion to those around them has become an increasingly problematic issue. Straterra is a non-scheduled medication. Its side effect profile is relatively easy to manage. In practiced hands, it has a very useful place in the treatment of ADHD. The National Association of Child and Adolescence Psychiatry has placed it on a first line basis to be used in equal efficacy and desirability with the two classes of stimulants. Straterra has been effective in about 60% of his patients.

Francine Harbour said she had Bipolar disorder. She also worked as a volunteer at the National Alliance for the Mentally Ill. Her path to wellness has taken 14 years. She started in the late 1980s and went through several different medications. After many years, she had such a build-up of symptoms that went unnoticed that she attempted suicide. She was then put into Southcentral Counseling and finally received the full spectrum of continued care that she needed. She asked a rhetorical question that the committee might want to discuss later in the meeting. What would the committee do if, after they disbanded, the Legislature deleted the "medically necessary" provision for prescriptions? All the great

works that the committee is doing can be washed away if the Legislature decides to delete or amend the provision. It would behoove the committee to realize that this is not cast in stone and can be changed by the Legislature.

Jeffrey Hill, Eli Lilly, discussed Duloxatene in the treatment of depression and Adamoxatine in the treatment of ADHD. Duloxetine is a selective serotonin and norepinephrine reuptake inhibitor. It is a balanced and potent inhibitor of both serotonin and norepinephrine reuptake. And this is thought to be the source of its rapid onset of activity, its efficacy in treating a broad range of depressive symptoms and its high remission rates. In clinical trials, Duloxatene showed rapid improvements in treating the symptoms of depression with significant improvement seen within one to two weeks of therapy. At the first week of therapy, Duloxetine showed statistically significant improvements in the core emotional symptoms of depression. At the second week of therapy, Duloxatene showed statistically significant separation on the primary efficacy measure, which is the HamD-17. It is recognized that successful treatment of depression should address both the emotion and physical symptoms of the disorder. Studies show that many depressed patients experience painful physical symptoms, including vague aches and pains, backaches and neck and shoulder pains. The DSM4-TR has recognized these symptoms as an associated feature of a depressive episode. Failure to accurately diagnose and treat these physical symptoms of depression may have negative clinical and economic consequences. Duloxatene's balanced and dual activity on serotonin and norepinephrine is thought to be the source of its efficacy in treating both the emotional and physical symptoms of depression. Remission is the goal of antidepressant therapy. And the goal of therapy is for patients to become symptom free and return to normal functioning. In clinical trials, Duloxetine showed high rates of remission. At nine weeks of therapy, 44% of patients achieved remission at a 60 milligram, once daily dose. Duloxetine offers important clinical advantages in the treatment of depression. It is effective in treating a broad range of depressive symptoms, both emotional and physical. It has a rapid onset of antidepressant activity. Duloxetine offers an opportunity for many patients to achieve remission. Clinical studies show that Duloxetine is safe and well tolerated. These clinical advantages provide support for Duloxetine's inclusion as a preferred agent on the preferred drug list. Atomoxetine represents a new class of therapeutic agents in the treatment of ADHD. It is a selective norepinephrine reuptake inhibitor. As well as having a direct effect on the levels of norepinephrine in the brain, Atomoxetine also increases the levels of dopamine selectively in the pre-frontal cortex. This is important, because both norepinephrine and dopamine have been widely implicated in AHDH and the pre-frontal cortex is thought to play an important role in the disorder. Atomoxetine's mechanism of action gives it unique clinical properties that offer advantages in several important patient groups with ADHD. In clinical trials, Atomoxetine showed significant improvements in both the core symptoms of ADHD as well as in the hyperactive, impulsive and inattentive symptoms of the disorder. Anxiety disorders are common in ADHD patients. Psycho-stimulants may worsen these conditions that are contraindicated in these patients. Atomoxetine does not carry this contraindication. In fact, there is evidence suggesting that Atomoxetine improves tics and anxiety symptoms in ADHD patients with these symptoms. Comorbid substance use disorders are present in up to 30% of ADHD patients. Many clinicians may be reluctant to prescribe psycho-stimulants because of their potential for abuse and dependence. Psycho-stimulants are scheduled two controlled substances and should be used cautiously in patients that have a history of alcohol and drug abuse. Atomoxetine is not a controlled substance and has been proven to lack of abuse potential. Studies show that Atomoxetine does not produce physiologic subjective effects indicative of an abuse liability. For these reasons, it is not likely that Atomoxetine will be abused, misused or diverted. Atomoxetine may be preferred in patients with a history of alcohol and drug abuse. Atomoxetine is the only FDA approved non-controlled, non-stimulant medication available in the treatment of ADHD. Additionally, it is the only proven alternative to the psycho-stimulants and it is potentially a preferred

agent in easily identifiable patient populations. Atomoxetine's unique mechanism of action, its clinical efficacy and its therapeutic benefits offer support for its inclusion as preferred agent on a preferred drug list.

Jenette Grasto, NAMI Fairbanks, said the doctors needed the option to use all the tools that are available to them when treating mental health patients. She spoke to the committee about the human side, rather than the technical aspects, of prescribing drugs for mental illness. When she was at college, she volunteered at the state hospital and saw people that were warehoused instead of treated. Her brother has suffered from schizophrenia for 23 years and she watched him go through all the problems with all the older anti-psychotics. Her children have the option of using up-to-date medications and current treatment to achieve recovery. Her nephew with untreated depression decided not to live anymore and did not even reach his 26th birthday. The thing about mental illness is people can overcome the illness and go on to live a full life and society needs to give them the chance to do that. This will often depend on their wiliness and ability to access effective medications. Some of the problems with psychotropic meds are the side effects. If the side effects are too severe, it often leads to poor compliance. The quality of life of the consumer needs to be considered. The burden to society of untreated mental illness, including increased costs of hospitalization, jail and suicide, needs to be considered. Mental health drugs are dependent on trial and error and they cannot be standardized. The doctor absolutely needs to use the best drugs at their disposal. If this program puts more burdens on the doctors, the consumers are the ones that will suffer, which is unacceptable.

Traci Barbee, the executive director of NAMI Alaska, said it was important to keep the physicians' choices open. She was involved with NAMI Alaska, because her son has ADHD and Bipolar disorder. They spent six years trying to find the appropriate medication for him. Once they took their son camping and he imagined flies swarming around his head and spent the entire weekend in the camper with a blanket over his head screaming about the flies. That is one small example of the way her son spent the majority of his childhood until they found the medications that worked for him. Her son is currently a relatively normal senior in high school and is doing well. She reiterated how important it was to keep these options open. Every day she works with mentally ill people. Without these options, they do not have a chance of recovery.

GREGORY POLSTON MOVED TO EXTEND THE PUBLIC COMMENTS. SECONDED BY THOMAS HUNT. CHAIRMAN BRODSKY CALLED FOR DISCUSSION OF THE MOTION.

Thomas Hunt felt that psychotropic drugs had been adequately covered and he asked the remaining speakers to address other medications. Alexander vonHafften felt everyone who wanted to speak should have the opportunity. Diane Liljegren noted that the committee would not be able to cover all the drug classification on the agenda if the public comments continued on much longer. Chairman Brodsky felt the public's input was important to the process.

CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED WITH DIANE LILJEGREN OPPOSED.

Shamal Das, a cardiovascular medical scientist, discussed Crestor. Outcomes are a class effect. Not all trials have shown outcomes, because the populations and trials are different. The most important predictor of the outcome of trials is LDL. When Lipitor came on the market there was no outcome trial. Crestor offers the advantage of an outcome trial. The 10-milligram starting dose gets 80% of patients to goal with a 50% reduction in LDL. The other advantage of Crestor is that it lowers the CRP, which is

becoming an important predictor. He discussed several outcome trials. In head-to-head trials, Crestor at 10 milligrams lowered LDL the same as a 40 milligrams of Lipitor. When looking at Statins, you want a lower dose, because digression is a major problem. He discussed the safety aspect of Crestor. Crestor is a very safe drug. 10 million prescriptions of Crestor have been written worldwide and there have been no deaths. There are about 4 million patients on Crestor. He felt it was important to have Crestor available so the physicians can have the choice of treating their patients aggressively.

Aaron Middlekauf said he was an active duty pharmacist at Elmendorf Air Force Base. The Department of Defense (DOD) and Veterans Administration (VA) decided to select Zocor as their single high potency statin. The DOD determined that 50% of LDL reduction attainable with Zocor conferred to 90% of our patient population being able to reach the incept goal. We also wanted to establish continuity of care and uniformity across our system, as well as between systems, to improve cost effectiveness of lipid lowering drug therapy. Cost savings for Zocor was established by a contract with MERCK. The generic product will be commercially available at the end of next year.

Dan Heincy, a pharmacist and director of government affairs for MERCK, discussed Zocor. Zocor enjoys formulary status almost universally in Alaska. It is covered under the Native Health Act, the military and it has a high penetration within the Medicaid market. Zocor is a safe and effective drug and will be going generic very soon. There are many reasons why Zocor should be on the preferred drug list: convenience for the patients that are currently using Zocor, the fact that it will be going generic and the safety profile. There was one thing on the safety profile that was a little disturbing. A previous speaker mentioned the PROVE-IT study versus the A to Z study, which we have some real concerns with. You cannot compare studies that are not similar studies. The PROVE-IT study used Lipitor versus Pravachol. The A to Z study was two different arms using two different strengths of Zocor. As a result of that study there really wasn't anything new that came out. The FDA has actually issued some statements on that study, which the committee should review. As an example, in the A to Z study, the incidents of myopathy was .4% for Zocor 80. There were nearly 45,000 patients in the A to Z study and there were only three confirmed cases of rhabdomyolysis. All three of those patients had other significant factors. In one case, it was a dosage of a drug that should not have been given with any statin. He read a statement with quote when quoting the FDA. In addition, there's been news articles reported that the FDA has publicly stated that the rate of muscle related adverse events would have been expected based upon data from other Statin studies. "Several of the patients who developed serious muscle injury had well known contributing and complicating factors." The FDA said, "We believe that the labeling for Zocor adequately can phase the balance of risks and benefits across the dosage range approved and contains adequate information for safe use." The A to Z study showed the same as the PROVE-IT study that using higher doses of Statins does reduce LDLC, which is what you want to do according to the new guidelines, but there is no new information about safety of efficacy that can be drawn from those studies. To try to compare those studies is like taking apples and oranges.

Andrezej Maciejewski said he was born in Poland and graduated from medical school in 1979. He became a researcher in pharmacology and a teacher in Poland. He later moved to Germany where he conducted cardiovascular research at the University of Heidelburg. After that, he went to San Diego to work at UCSD in pharmacology and hypertension. He completed his training and moved to Alaska three years ago as a nephrologist and internal medicine specialist. He did not sponsor any company and was not paid for his testimony. He was representing the medical community and Alaskan patients. There is no doubt that Statins work and preserve diseases. Medications that we have at our disposal are our weapons or tools that we fight diseases with. The evidence of positive effects of reducing morbidity and mortality when it comes to Statins is so great that there was a fairly well known recommendation

that they should be added to drinking water. Surgical specialists, especially cardiovascular surgeons, prescribe Statins after bypass surgery to those patients that never received it before. There is overwhelming evidence of acceptance of using Statins and their outcomes. He prescribes all of them including Crestor, Lipitor, Pravachol, Vytorin and Zocor. He likes to prescribe all of them, therefore he would like to ask the committee not to exclude any of those drugs from the preferred drug list. It is important that the physicians do not have to write "medically necessary" when prescribing those agents, because it is obvious that they all work and they are all needed. We should have all of them on the preferred drug list, because doctors prescribe all of them. The relationship between a physician and a patient is based on that initial decision that the doctor writes on the prescription. The patient has a lot of faith in that particular agent. A drug that is being changed by the pharmacy or a preferred drug list loses its power and compliance drops due to their doubts. If we criticize politicians for trying to reduce weapons of mass destruction, how can we criticize anybody who develops such weapons? All the agents should remain on the preferred drug list.

In response to Thomas Hunt, Andrezej Maciejewski said there was still a lot to be learned from experiences with Statin agents. For example, a few months ago there was a criticism that Crestor might be harmful to the kidney. There is recorded evidence that what they considered negative was actually positive. Crestor has a preserving ability for the kidneys. An earlier speaker said Pravachol's evidence of mortality was excellent. It has a long history and has been well studied. Even if it is weak, it still has an excellent rate at reducing mortality. There are things that we do not know and aspects of our pharmacological agents that we are still learning about. Therefore, limiting them will cause a loss of future experience.

Maria Kootsikas discussed Ambien, a non-benzodiazepine. Ambien has been well studied in many randomized double blind placebo controlled trials for efficacy up to 35 days. The package insert states for its indication that Ambien has been shown to decrease sleep latency and increase duration of sleep up to 35 days in controlled clinical trials. Ambien improves time to sleep, number of awakenings and quality of sleep for transient and chronic insomnia. Ambien is well studied in the elderly, depressed, patients takings Prozac, and in travelers crossing five to eight time zones. It has a half-life of 2.5 to 3 hours, resulting in a full night's sleep of 6 to 8 hours. Ambien has no active metabolites and has a sleep latency of 20 to 30 minutes. Ambien is a non-benzodiazepine selectively inhibiting omega(1) or benzodiazepine 1 receptors, thus it does not have anti-convulsing properties and does not effect sleep architecture. This is of importance especially in the elderly who have less stages 3 and 4 state, which are needed for physical restoration. Ambien has been available since 1993 in the U.S. It has more than 10 years of U.S. experience with 14 years worldwide. In short-term studies, statistical significant ADRs less than 2% were drowsiness, 2% dizziness, 1% in diarrhea. It was found that a dose of 10 milligrams, which exceeds the recommended dose, did not increase frequency of confusion in the elderly. If ADRs are seen in the elderly, it will be at the higher doses and not at the recommended dose of 5 milligrams. Ambien is category B, whereas the other benzodiazepine are category X. Post marketing surveillance studies are an important source for evaluating the safety of a product once it is prescribed. In a three-year post marketing study, Ambien had a similar safety profile to the pre-marketing trials. In randomized placebo controlled trials, the following had been minimally reported: daytime residual effects, memory impairment, rebound insomnia tolerance. Germany has an epidemiological devised database known as the Early Warning System, which is a method to record and quantify abuse patterns of chemical substances. Between 1992 and 1997, 4.5 cases of abuse were reported for Ambien per 10,000 doses, which was significantly less than the 106.7 reported per 10,000 doses of benzodiazepines. In Europe, the doses are much higher and they are utilized up to 40 milligrams. Almost all cases were patients with a history of drug, alcohol abuse and/or psychiatric disorders. Alcohol abuse, drug abuse,

depression and other psychiatric (indiscernible) are significantly associated with patients who have insomnia. For example, alcohol abuse is twice as likely to be associated with a person who has insomnia. A recent study published in August 2004 in the Journal of Clinical Psychiatry showed that Ambien dosed from 3 to 5 tablets a week, in a 12 week study, showed significant improvement in total sleep time without evidence of diminishing effectiveness. The patients actually limited themselves to 80% of the available medication. Ambien treats insomnia, which is highly associated with depression, without treating or worsening the patient's depression. It allows the patient to sleep and concentrate better with an improved quality of life. There is evidence that Ambien increases a patient's total sleep time and the quality of life for patients taking SSRIs without effecting their depression. There is minimal risk for abuse and tolerance compared to the benzodiazepines, especially for patients with psychiatric disorders and drug abuse.

Sherry Dodd, Janssen Medical Affairs, discussed the long-acting opiates. She applauded the committee for their work, especially the "medically necessary" provision. However, from earlier comments it sounds like there could be problems with that provision. The chronic pain population is inherently at risk, because chronic pain is under treated in general, especially for at-risk populations like the elderly and the poor. When you have a change in the preferred drug list, patients are not grandfathered. A patient who is doing very well on a chronic pain therapy may be forced to change medications, which requires a visit to the doctor and incurs a lot of health care resources. These patients do not do well when they are forced to change a medication that is helping them. We also know that opiate rotation is common among these patients, because they develop a tolerance and need different types of chemicals. A preferred drug list that is broader and allows patients to move from one medication to another is more beneficial. The Oregon Health Policy Center is involved in evidence-based medicine and they are trying to do a good job of bringing together all the data. However, they look at clinical and safety evidence, but they have no allowed economic evidence. To really bring all these things together requires rigorous scientific mythological modeling that allows one to look at clinical efficacy and effectiveness, safety and utilization and cost drivers. Until we get to that point, it is very difficult to determine what will be the most cost-effective therapy. The Oregon Department of Human Services put out a report in early 2000 about an increase in Methadone related deaths from chronic non-malignant pain use versus drug maintenance. The problem she had with the Oregon based review process, as well as First Health, is that a lack of evidence for superiority does not mean equality. As you look at the reports, you should know that they are not putting everything in together and some of their recommendations have been problematic. There are 44 Medicaid states that have Duragesic as the preferred medication or equal access to the other drugs. Duragesic has the same indications as all of the long-acting opiates therapies. It is for chronic non-malignant pain. Patients do not have to fail an oral first. It is a trans-derminal delivery system that has been available for over 10 years. Duragesic is fentanyl based and is not a morphine or oxycodone. It has a unique delivery system and it offers the choice of a patch that is used once every three days versus multiple pills per day. This is an important option for chronic pain patients. Duragesic should be part of the preferred drug list as a frontline drug. The APA Guidelines still stay that Morphine is standard, unless there are drugs that have longer duration of therapy and a better safety profile, which Duragesic offers.

David Samson, a local psychiatrist, said he has worked at Anchorage Community Mental Health Center as well as other centers around the state. He was concerned about this process and the safety of his Medicaid patients. The medical necessity is a wonderful thing, if First Health and the State of Alaska could be trusted to keep that in place. People are already receiving friendly letters from First Health that they are not prescribing medications on the preferred drug list. He was concerned that those friendly letters would turn into less friendly letters and eventually the preferred medications would be pushed

harder. The providers who have a majority of mental health patients, such as Southcentral and Anchorage Community Health Center, have doubled their patient load in the last five years, yet their budget has been cut 6% over that same period of time. We cannot provide the other services in our community settings to provide the other necessary treatments. He was also concerned about generics. Generics are bio-equivalent from a range of 80-120% of the branded products. Patients do not always get the same generic medications from different pharmacies, which can be a dangerous thing for mental health patients. Our evidenced-based process, especially for psychiatry, is less than perfect. The Statin bundle today is about an inch thick and the combinations of all the psychiatric medications are less than half an inch thick. There is very little evidence to base a good scientific decision on. The decision should remain between the physician and the patient. The evidence-based information is somewhat in question. He was bothered by page 7 of the PDL backup material for sedative hypnotics, which contain a few minor errors. He hoped the medical necessity clause would be maintained.

Leon Chandler said he was the owner and operator of the AAA Pain Clinic. It is imperative that we have access to the medications to treat various diseases. People with mental illness have significantly decreased their ability to get health care insurance. The lucky ones end up on Medicaid and the others have to pay for their own treatment. (Indiscernible -- telephonic, unable to hear.) He applauded the efforts of the P&T Committee, but wanted them to understand that access to care was imperative for the patients who had to live with their pain. He asked that the preferred drug list maintain a wide variety of drugs for physicians to prescribe.

Chairman Brodsky closed the public comment session of the meeting.

Dr. Helfand responded to the earlier comments about the Oregon Evidence Based Practice Center. All the recommendations were made by a committee, which is similar to the P&T Committee. Several states have used our reports and come to different conclusions, because once they know what the evidence does and does not say, they can apply different values or clinical judgments to that evidence. He agreed with the previous speaker regarding the economic evidence. In some settings, people want to use economic analysis to make their judgments. Other groups want to have the decision made entirely on safety and efficacy and then apply the economic issues afterwards. The reason our reports do not review economic analyses is because the people who fund our reports have not asked us to. We would be happy to do it if they were interested in using that information. If you are going to introduce economic analyses into the discussion then it should be introduced in a systematic way to allow you to critically review all of the information.

V. HMG-CoA REDUCTASE INHIBITORS (STATINS)

Chairman Brodsky welcomed Dr. Helfand to the meeting. The P&T Committee has elected not to use economic information in their decision making. They have used the evidence for efficacy and other effects. Terry Babb, a former member of the committee, will be replacing Sandy Kapur as the First Health representative.

Terry Babb said the committee would be looking at the high potency Statins, Atorvastatin, Simvastatin and Rosuvastatin, separately. The remaining Statins would be reviewed separately. We asked Dr. Kutchera, a cardiologist, for his recommendations. He said he recognized the value of using all Statins. He selects Statins based on factors such as the formulary for someone in the Department of Defense or someone who needs a less expensive drug because they are paying cash. Dr. Kutchera sees value in Pravastatin, specific to the lack of drug-drug interactions. He recognizes the value of the high potency

Statins and their ability to get to goal. Statins competitively inhibit 3-hydroxy-3methyl-glutaryl-coenzyme A (HMG-coA) reductase. It is a rate-limiting step in cholesterol biosynthesis. All Statins can effectively lower LDL, total cholesterol, triglycerides and increase HDL. The one notable exception is Atorvastatin 80 milligrams, which has more variable effects on HDL. There is much evidence that many of these things are considered class effects. For example, contraindication warnings and major adverse events are very similar amongst the group. As a single agent, the HMG-CoA reductase inhibitors are comparable to, or more effective than, bile acid sequestrates and are being used as the initial drugs of choice for patients with primary hypercholesterolemia. However, a number of patients will not be optimally controlled with monotherapy. In these patients, an enhanced effect can be obtained by combining the drug with other lipid lowering agents such as bile acid sequestrates. The Department of Veterans Affairs formulary includes Fluvastatin immediate release oral, Fluvastatin sustained action oral, Lovastatin tablets and Simvastatin tablets. The summary of the pipeline agents expected to offer related treatment options includes Pitavastatin. Pravastatin brings advantages specific to the lack of drug interactions. Both Fluvastatin and Rouvastatin are not indicated for children. Atorvastatin and Fluvastatin work nicely with patients with renal dysfunction. Atorvastatin, Lovastatin, Pravastatin and Simvastin all reduce cardiovascular events. Atorvastatin and Simvastatin reduce cardiovascular events in patients with low LDL. All Statins have similar risks versus benefits.

Dr. Helfand discussed the A to Z Trial, which was not contained in the Oregon Evidence Based Practice Center information, because it was so new. The A to Z Trial was two different strategies for using Simvastatin in patients who have potential MIs or other acute coronary syndromes. Neither of those strategies was as aggressive as immediate Atorvastatin 80 milligrams, as was the strategy in the PROVE-IT Trial. The A to Z Trial compared 40 milligrams of Simvastatin increased to 80 milligrams after several weeks, which was not comparable to immediate 80 milligrams of Atorvastatin. So we still do not know what a 80-milligram-to-80-milligram study would show. There were 5,000 patients in the Z component of the A to Z Trial. Nine patients who received 80 milligrams of Simvastatin developed chemical evidence of myopathy and three of them had severe (indiscernible) and additional risk factors. There is no prior reason to suspect that Simvastatin would have a higher rate of (indiscernible) than other statins. In fact, there have been several head-to-head trials that have not shown an increased risk of anything with Simvastatin compared to others. The PROVE-IT Trial demonstrates that high potency, high dose Atorvastatin has much better benefits than risks for post MI patients. The first phase of the A to Z Trial where they used 40 milligrams of Atorvastatin against a placebo really did demonstrate a benefit. The second phase where they had 80 milligrams, compared to 20 milligrams in the other group, had a strong trend toward a mortality benefit.

Thomas Hunt said he appreciated the distinction between the high and low potency Statins, because it made the decision somewhat easier. He did not feel they had heard convincing evidence in efficacy or safety between the three high potency agents. He felt they were probably therapeutically equivalent.

Chairman Brodsky said the literature did not indicate any significant differences between the drugs. He challenged the drug industry to do more head-to-head trials to help physicians make better decisions.

Thomas Hunt said all three of the high potency Statins reduced LDL. Reducing LDL will generate better mortality statistics. We can achieve goal with all three of the agents when dosed at various levels. The safety data on the Statins is incomplete.

THOMAS HUNT MOVED THAT THE THREE HIGH POTENCY STATIN AGENTS WERE THERAPUTICALLY EQUIVALENT. SECONDED BY GREGORY POLSTON. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION.

In response to Heidi Brainerd, Chairman Brodsky said each classification would be review on a yearly basis. If breakthrough information or new products became available then that could be brought back to the committee. He discussed the Statins with a cardiologist this morning and he indicated that one of the high potency Statins should to be available, but it did not matter which one.

CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

The P&T Committee then moved on to consider the low potency Statins including Lovastatin, Pravastatin and Fluvastatin.

Diane Liljegren suggested including Pravachol to the preferred drug list.

Dr. Helfand said both Pravachol and Lovastatin have been proven to reduce cardiovascular events in low risk populations. Pravastatin has theoretical advantages because it has fewer interactions in certain groups of patients. This would be more of a practical decision than an evidence-based decision, because they are both effective and safe drugs according to the evidence.

Chairman Brodsky reiterated that they were developing a preferred drug list and not a formulary. All drugs will be available if the physician writes "medically necessary" on the prescription, although we prefer people to use the drugs on the preferred drug list if we deem them equivalent.

Diane Liljegren felt it was important to keep the process simple. As a physician, she would prefer to make choices that would minimize her need to write "medically necessary" on prescriptions.

In response to Representative Wilson, Chairman Brodsky said there was no plans to change the medical necessity clause. We have been successful so far with 80% compliance. There have been cost savings and hopefully that will allow us to keep providing benefits to the Medicaid population as the population and drug costs grow. Classifications will be periodically re-reviewed to make sure there is no new evidence to show certain drugs should be added or taken off the preferred drug list.

ARTHUR HANSEN MOVED THAT THE LOW POTENCY STATINS BE CONSIDERED EQUIVALENT. THE MOTION WAS NOT SECONDED.

THOMAS HUNT MOVED TO INCLUDE PRAVACHOL AS A LOW POTENCY STATIN ON THE PREFERRED DRUG LIST. SECONDED BY DIANE LILJEGREN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

VI. LONG-ACTING OPIATES

Terry Babb said the three long-acting opiate classes were Oxycodone, Fentanyl and the four Morphine products including MS Contin, Oramorph, Kadian, and Avinza. The narcotic of choice is determined by dosage formulation, patient convenience and side effects; not by presumed lack of potency. There is

some question whether or not the peak-to-trough fluctuation has a clinical benefit. MS Contin has a duration of 8 to 12 hours, Kadian is 12 to 24 hours and Avinza is 24 hours. The clinical significance of a wide or narrow peak-to-trough fluctuation is still unclear. We need to look at a dosage interval that is adequate so patients can get sufficient sleep, which is the goal.

Gregory Polston noted that there was a difference between how the three medications were delivered.

Terry Babb said the contraindications, warnings, major adverse events and drug interactions were all somewhat similar and considered class effects. The Department of Veterans Affairs formulary current has Fentanyl, Methadone, Morphine and Oxycodone. Exceptions to the class include Fentanyl has a pediatric indication for opiate tolerant children greater than 2 years of age. Avinza, in extremely high doses, can increase fumaric acid. Kadian and Avinza are available in pellets, which allows the capsules to be opened up and sprinkled on applesauce. There has been very limited head-to-head studies. Between Fentanyl and Oramorph, Fentanyl has shown greater pain relief, decreased constipation and increased quality of life. Avinza and MS Contin have a very comparable efficacy, although Avinza in the morning demonstrated improved quality of sleep.

Dr. Chou discussed the head-to-head trial of Fentanyl versus Oral Morphine, which was a poor quality trial. It was unblinded and most of the patients had failed or been on oral Morphine before. We do not feel that trial gave unbiased results. There is another study of oral Morphine versus Fentanyl that is in progress, but we have not seen a fully published report yet.

Chairman Brodsky said an earlier speaker had noted that the Fentanyl patches were harder to abuse, but they have seen some patients cutting up the patches and chewing them.

Gregory Polston pointed out that there was a difference in the three Morphine drugs. Patients respond to medications differently and there are different delivery systems. Some people do not want to take pills while other people prefer taking medications less frequently. Being able to take a pill to immediately control pain allows people to take control of their lives. Unlike the Statins, we do not have a marker to look at LDL or other things.

Thomas Hunt and Gregory Polston discussed the differences in the Morphine products. Gregory Polston said none of the Morphine products had been proven superior, so they are equivalent. However, certain patients have shown different responses to these drugs. Thomas Hunt said he was not convinced that there was a substantive difference between the Morphine products that should sway the committee one way or the other. Gregory Polston discussed some of the differences such as a patient who had more pain in the morning might prefer Avinza or other patients might prefer taking only one pill a day so they could go about their lives. Narcotics are not antibiotics. They do not cure the pain problem and patients continue to have pain after the medication wears off. By rotating the drugs when they stop working, a physician can avoid increasing doses. Thomas Hunt said they could simplify and maintain the rotation strategy by keeping one Transdermal system, one Oxycodone system and one Morphine system, rather than keeping all three Morphines. Gregory Polston felt they needed all three of the Morphines.

Ronald Miller pointed out that all medications were available by writing “medical necessity” on the prescription. He suggested selecting one of the Morphine products as a starting point.

Robert Carlson pointed out that they were discussing the art of medicine rather than the science of medicine. As long as the medical necessity option is available there is nothing to worry about. The

committee is being asked to simplify the preferred drug list, but the practitioner always has the ability to deviate from it.

Chairman Brodsky said a generic medication would not automatically be added to the preferred drug list due to pricing issues. Sometime the rebates are greater for non-generic products.

Gregory Polston felt the Morphines were equivalent, but OxyCotin and Duragesic were different products that should be available.

Kelly Conright said her clinical experience was that she had fewer side effects with OxyContin versus a sustained acting Morphine, but her patients did not go out on the street and sell their drugs.

Thomas Hunt did not feel the committee should consider the street value of the drugs.

Diane Liljegren felt there should be a grandfather clause for people who have been stabilized on one of the preparations. It can be a very uncomfortable and unpleasant thing to have to switch medications, even if the drug is within the same class.

Chairman Brodsky said the physician would have to write "medical necessity" on a prescription when prescribing a medication not on the preferred drug list. The medical necessity clause is similar to a grandfather clause, because the medication can still be prescribed.

THOMAS HUNT MOVED TO RETAIN THE LONG-ACTING FENTANYL PRODUCT, LONG-ACTING OXYCODONE PRODUCT AND DECLARE THE MORPHINE PRODUCTS THERAPEUTICALLY EQUIVALENT. SECONDED BY MARVIN BERGESON. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

VII. SEDATIVE/HYPNOTICS

Terry Babb said the Sedative/Hypnotics could be broken into three gross classes. Flurazepam, Quazepam and Estazolam all have longer half-lives. Temazapam and Triazolam both have shorter half-lives. Zolpidem and Zaleplon are both non-benzodiazepines. These can work on omega-1 or omega-2 receptors. All the positive effects come with the omega-1 and the negative effects come with the omega-2. The difference is that benzodiazepines affect both, so they illicit the positive effects, but they have been shown to have problems with cognition and memory depending on when the medications are taken. The non-benzodiazepines just affect the omega-1. They combine selectively with the omega-1 receptor. Although this theoretically proposes advantages, we really see few significant advantages in terms of the adverse effects. The DVA formulary uses Temazepam oral only. On July 15, 2004, the FDA accepted the resubmission of the NDA for the Estorra brand of eszopicione for the treatment of insomnia as a complete response and has begun its review. There are two significant side effects or treatment failures with sedative/hypnotics, rebound insomnia and early morning insomnia. Benzodiazepines have an extremely wide margin of safety, but a short half-life product should be discharged gradually. Temazepam offers some benefits in terms of it conjugated metabolism, which is good for the elderly. Benzodiazepines are contraindicated in pregnancy. Zolpidem is category B whereas Zaleplon is category C and Benzodiazepines are category X. From a pregnancy standpoint, that would favor Zolpidem. Non-benzodiazepines have no problems with patients with renal or hepatic dysfunction, although low doses are advised for all elderly patients. As far as comparative efficacy,

motor tasks and memory capabilities appear to be better with non-benzodiazepines. Zaleplon, at a 10-milligram dose, had a favorable outcome for memory preservation. It is widely understood that Zaleplon may have a better safety profile.

Robert Carlson agreed with Mr. Babb's comments about safety as long as the medications were taken as directed. However, there are people who take more than the prescribed number of sedatives. Thirty to 40 benzodiazepines can make a person groggy or dopey and 40 of the newer agents can be lethal.

Terry Babb said there was no question that the non-benzodiazepines were not as safe as the benzodiazepines. Benzodiazepines are both inhibitors and inducers of CYP450 3A3/4 whereas the non-benzodiazepines are only problematic with 3A4 inducers.

Alexander vonHafften referred to Dr. Morris' work in sleep disorders and the non-benzodiazepine compounds. He tried to avoid the use of benzodiazepines, even in the short-term. The first line is to try and promote sleep hygiene before prescribing a medication. He would consider using Trazodone, which were not considered in this class. Some of the literature referred to using Benadryl and some over-the-counter substances, but he was not sure what the evidence was to support that even though it was commonly done. He was concerned about some of the complications of the longer half-life benzodiazepines. His preferred agent would be Temazepam, which was commonly used at API when discharging patients. He felt the committee had done good work in the "medical necessity" clause. He referenced to a quote from Dave Campana on page 10 of the previous meeting minutes that said the criteria could be changed in the future as necessary. He questioned if all changes to the "medical necessity" clause would come before the committee for consideration.

Dave Campana said changes to the "medical necessity" clause would be determined by the P&T Committee. When we first started developing the program, we did not know what kind of support we would get from the physicians. Based on the first two months of utilization of the preferred drug list, we have 80% support for the program. We hope to eventually get to 90% support for the program.

Thomas Hunt noted that this item was not on the agenda and should be a separate agenda item at a future meeting.

Alexander vonHafften felt Temazepam and one of the non-benzodiazepine hypnotics should be included on the preferred drug list.

Sherrie Richey said of the non-benzodiazepines, they had the most experience with Zolpidem and pregnancy. During pregnancy, we prefer to use medications that have the most clinical experience in terms of numbers of patients that have been treated with the drug without documented adverse effects. There are a lot of pregnant women that have insomnia. She felt Zolpidem should be added to the preferred drug list.

In response to Terry Babb, Chairman Brodsky said he did not feel they needed two of the non-benzodiazepines on the preferred drug list.

Thomas Hunt did not feel Temazepam needed to be on the preferred drug list.

In response to Sherrie Richey, Terry Babb said there was a theoretical advantage for Temazepam when used in elderly patients in terms of conjugated metabolism.

Chairman Brodsky said there was a lot of theoretical evidence for many of these medications, but not a lot of practical outcome evidence or evidence-based support for this class.

Duane Hopson said psychiatrists generally used Temazepam.

THOMAS HUNT MOVED THAT TEMAZEPAM BE ADDED TO THE PREFERRED DRUG LIST IN THE BENZEDIAZEPINE CLASS. SECONDED BY ALEXANDER vonHAFFTEN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

SHERRIE RICHEY MOVED THAT ZOLPIDEM BE ADDED TO THE PREFERRED DRUG LIST IN THE NON-BENZEDIAZEPINE CLASS. SECONDED BY MARVIN BEREGSON. CHAIRMAN BRODSKY CALLED FOR DISCUSSION OF THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

In response to Michale Boothe, Chairman Brodsky felt the process should be followed and all the stimulants should be discussed separately as opposed to being lumped together.

VIII. SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)

Diane Liljegren said she had discussed this issue extensively with fellow physicians and felt all SSRIs should be preferred, because the response to SSRIs was unpredictable.

Kelly Conright said First Health should anticipate a lot of "medical necessity" prescriptions on the psych meds. She would not change any patients that were effectively taking psychotropic drugs, because it was not worth the risk.

Dave Campana said they could develop a grandfather clause for all patients currently using antidepressants, but all new prescriptions should follow the preferred drug list.

Alexander vonHafften said his clinical preference would be to have as much latitude as possible in this area. As a committee member, with assurance that the "medical necessity" clause would not be changed, he felt that every medication did not need to be included on the preferred drug list.

Duane Hopson noted that all of these agents were utilized. He felt they needed to be very sensitive to the community's request for open access to all of these drugs, which would include utilizing the "medical necessity" clause.

Chairman Brodsky said he had read extensively about SSRIs and passionately felt that there was a class effect. There was no scientific evidence that there was any difference. Not everyone responded to any individual drug, but 80% of people in clinical trials will respond to a particular SSRI. There are sometimes people who have adverse effects and other medications may need to be utilized. There is no evidence to say that there is anything but a class effect in this classification.

Alexander vonHafften agreed that there was a class effect on clinical effectiveness and side effects, but there are tremendous individual variations.

Chairman Brodsky said the variations could be handled with the "medical necessity" clause. We need to use the evidence to insure that we can continue the program. If we make everything preferred, we will lose the cost benefits and there will be a necessity to alter the Medicaid Program due to the increasing cost of drugs.

Sherrie Richey said in pregnancy and breastfeeding there are some potential differences that have been studied between Fluvoxamine and Sertraline, which are the drugs most commonly used. For the pregnant population, we need to use the SSRIs that have been on the market longer, because they have a lower adverse profile for breastfeeding mothers. We have a large population that are going to have postpartum depression issues, so it is important to consider these drugs in terms of breastfeeding and pregnancy.

Marvin Bergeson said newborn babies could have withdrawal symptoms with Fluoxetine.

Robert Carlson did not feel there was any reason to worry about the "medical necessity" clause as long as the P&T Committee did an annual review of the preferred drug list and the committee represented diverse groups within the State.

In response to Sherrie Richey, Chairman Brodsky said the strength of any system is that you elect your representatives and you have the right to voice your opinion to get the laws changed. The public comments were heard by the Health Department and the State Legislature, who created a program they felt would be effective based on consumers and the prescribing community. The program has been successful in saving money.

Sherrie Richey felt it was important that they did not use the "medical necessity" clause to prevent them from placing more than one drug for each class on the preferred drug list.

Chairman Brodsky said more generic and competitive drugs could be added to the preferred drug list over time.

Dr. Stillner said he was initially against the preferred drug list process, because the central nervous system is different than the pancreas. The process that has been established appears to be rational and has merit. He was happy to hear that anti-psychotics and mood stabilizers have been exempted from the system, which were many of the concerns expressed in the public testimony. The "medical necessity" clause seems like a reasonable vehicle for physicians to maintain their relationship with their patients. He suggested including all the antidepressants, excluding the SSRIs, and including Effexor, Wellbutrin XL, Cymbalta and all the generics, on the preferred drug list.

Alexander vonHafften said there were six major medicines in the SSRI classification. Three of those are generic and three are brand name. Two of the generics also have other branded formulations. He felt a good starting point would be adding the generics to the preferred drug list. He did not feel they needed to include the generic, as well as the branded versions of the generic.

Chairman Brodsky said including all the generics in the SSRI class might drive up the price. A generic could be more expensive and would not necessarily appear on the preferred drug list, unless the committee felt they had to have it.

Alexander vonHafften said he was opposed to including only one SSRI on the preferred drug list.

Heidi Brainerd noted that the committee had not discussed SSRIs in the pediatric population and questioned if there was an agent that had to be included for the pediatric population.

SHERRIE RICHEY MOVED THAT SERTRALINE BE ADDED TO THE PREFERRED DRUG LIST FOR THE PREGNANT POPULATION, PATIENTS CURRENTLY ON SSRIs BE GRANDFATHERED FOR THEIR CURRENT FORMULATION AND OTHERWISE DEEM THE SSRIs TO BE EQUIVALENT. SECONDED BY GEORGE STRANSKY. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION.

Diane Liljegren said she would prefer to have each portion of the motion considered separately, because each portion of the motion was a separate issue.

Sherrie Richey withdrew the motion. George Stransky withdrew his second of the motion.

SHERRIE RICHEY MOVED THAT SERTRALINE BE ADDED TO THE PREFERRED DRUG LIST. SECONDED BY ARTHUR HANSEN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION OF THE MOTION.

Chairman Brodsky said adding Sertraline to the preferred drug list would probably increase the cost for the entire class, because it was one of the more expensive drugs on the list. Sertraline could be prescribed by using the "medical necessity" clause.

Robert Carlson said the number of people with depression in Alaska was enormous, whereas pregnant women with depression was a small portion of the population. Physicians could treat a larger Medicaid group if the committee was careful in their expenditures. He felt the "medical necessity" clause should be used when prescribing Sertraline.

CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION. THE MOTION FAILED.

RONALD MILLER MOVED TO ACCEPT THE SSRIs AS EQUIVALENT. SECONDED BY GEORGE STRANSKY. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION.

The Committee discussed the advantages and disadvantages of the medications in the SSRI class. Terry Babb noted that the classification would be re-reviewed in a year and could be changed at that time. Diane Liljegren said she would like to see at least three SSRIs on the preferred drug list. Thomas Hunt felt they could call the SSRI agents therapeutically equivalent as long as they elected to use a grandfathering clause for those patients who were currently using SSRIs.

AN UNIDENTIFIED MALE MOVED TO AMEND THE MOTION TO INSURE THAT AT LEAST THREE SSRIs WERE INCLUDED ON THE PREFERRED DRUG LIST. SECONDED BY MARVIN BERGESON.

Thomas Hunt pointed out that class effect and interchangeability were not the same thing. He asked if there was an assumption that class effect implied interchangeability.

Chairman Brodsky said a class effect meant there was a reasonable probability that the drugs were interchangeable. When we say there is a class effect, First Health determines which drugs will be on the list based on the bids they receive from the pharmaceutical companies. It could include one drug, all the drugs or anything in between. If a patient needs a drug that is not on the preferred list then the physician can use the "medical necessity" clause.

CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE AMENDMENT TO THE MOTION TO INCLUDE AT LEAST THREE SSRIs ON THE PREFERRED DRUG LIST. THE MOTION PASSED WITH TWO OPPOSED.

CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION AS AMENDED, TO DEEM THE SSRI CLASS THEREPEUTICALLY EQIVALENT AND INCLUDE AT LEAST THREE DRUGS ON THE LIST. THE MOTION PASSED WITH 8 IN FAVOR AND 4 OPPOSED.

ROBERT CARLSON MOVED TO GRANDFATHER PATIENTS CURRENTLY USING SSRIs. SECONDED BY MARVIN BERGESON. CHARIMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED UNANIMOUSLY.

Chairman Brodsky noted that the remaining items on the agenda would have to be postponed to the next meeting, but no public testimony would be taken on those items. They would accept public testimony prior to each new classification at the next meeting.

Terry Babb reviewed which drugs would be included on the preferred drug list as a result of this meeting. High potency Statins: Crestor and Zocor. Low potency Statins: Pravastatin and Lescol, Lescol XL and Lovastatin. Sedative/Hypnotics: Flurazepam, Estazolam, Temazepam, Triazolam and Ambien. SSRIs: Fluoxetine, Lexapro and an undetermined drug. Long-Acting Opiates: Avinza, Kadian, Oramorph, OxyCotin and Duragesic.

RONALD MILLER MOVED THAT THE SSRI CLASS BE REVISITED SIX MONTHS FROM THE IMPLEMENTATION DATE. SECONDED BY ARTHUR HANSEN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. THE MOTION PASSED WITH ONE OPPOSED.

Dave Campana said the next meeting was scheduled for October 22, 2004. The date of that meeting might be changed, because Chairman Brodsky would not be available.

Chairman Brodsky noted that the meeting minutes from the last meeting would be approved at the October meeting. He asked everyone to keep their materials so the items they did not get to at this meeting could be reviewed at the October meeting.

The meeting adjourned at 12:27 p.m.